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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/559,986	09/11/2006	James McCarthy	3712036.00667	6606

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EXAMINER	
SWOPE, SHERIDAN	
ART UNIT	PAPER NUMBER
1652	

NOTIFICATION DATE	DELIVERY MODE
08/10/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

chicago.patents@klgates.com

Office Action Summary	Application No.	Applicant(s)	
	10/559,986	MCCARTHY ET AL.	
	Examiner	Art Unit	
	SHERIDAN SWOPE	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *May 5, 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-44* is/are pending in the application.

4a) Of the above claim(s) *5-16 and 22-44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 17-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' Request for Continued Examination of May 5, 2010, in response to the action of November 5, 2009, is acknowledged. The currently pending claim set was filed June 6, 2009. It is acknowledged that no claims have been cancelled or added, while Claims 18-21 have been amended. Claims 1-44 are pending. Claims 5-16 and 22-44 were previously withdrawn pursuant to 37 CFR 1.142(b). Claims 1-4 and 17-21 are hereby reexamined.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Utility

Rejection of Claims 1-4 and 17-21 under 35 U.S.C. 101/112 because the claimed invention lacks patentable utility, for the reasons explained in the prior actions, is maintained.

In support of their request that said rejection be withdrawn, Applicants provide the following argument. It is not necessary that applicants prove the biological mechanism by which the claimed polypeptide operates in order to show utility. All that is required is that the claimed isolated peptides have a utility as has been disclosed throughout the specification and as demonstrated in the Examples. Applicants respectfully submit that the claimed polynucleotide (SEQ ID NO: 1) has a specific and substantial utility because it encodes the cysteine protease of SEQ ID NO: 2 (CcCP-1). Given that CcCP-1 is expressed at a high level in grain tissue and at a low level in the pericarp, it can be used, for example, by a skilled artisan to differentiate the two tissue types (see, specification, pages 26-27). As such, the claimed polynucleotide and polypeptide have a significant and presently available benefit to the public.

This argument is not found to be persuasive for the following reasons. It is acknowledged that it is not necessary that applicants prove the biological mechanism by which the claimed polypeptide operates in order to show utility. Nonetheless, the specification or art must provide a specific, substantial, and credible utility for the recited polynucleotide to be patentable. For the reasons explained in the prior actions the skilled would not conclude that, more likely than not, the polynucleotide of SEQ ID NO: 1 encodes a cysteine protease.

It is acknowledged that the specification discloses that CcCP-1 mRNA is expressed at a high level in grain tissue and at a low level in the pericarp of ripe C. arabica beans (pg 26-27; Fig 1&2). However, the CcCP-1 polynucleotide encodes the polypeptide of SEQ ID NO: 46, not the polypeptide of SEQ ID NO: 2. Therefore, said pages and figures of the disclosure do not provide a utility for the polynucleotide of SEQ ID NO: 1 or polynucleotides encoding SEQ ID NO: 2, as recited in the instant claims.

For these reasons and those explained in the prior actions, rejection of Claims 1-4 and 17-21 under 35 U.S.C. 101/112 because the claimed invention lacks patentable utility, is maintained.

Claim Rejections - 35 USC § 112-First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

Rejection of Claims 1-4 and 17-21 under 35 U.S.C. 112, first paragraph/enablement, for the reasons explained in the prior action, is maintained.

In support of their request that said rejection be withdrawn, Applicants provide the following arguments. These arguments are not found to be persuasive for reasons stated in each reply.

(A) In the BPAI precedential decision Ex parte Kubin, reversing the Examiner on a finding of lack of enablement with respect to appealed claims directed to an isolated nucleic acid encoding a polypeptide at least 80% identical to the amino acids set forth in SEQ ID NO:2 (a large protein of 365 amino acids), where the polypeptide binds CD48, the Examiner stated that while:

> "...molecular biology is generally an unpredictable art (and thus was so at the tame the application was filed).., the other Wands factors weigh in Appellants' favor, particularly "the state of the art" and "the relative skill of those in the art," In re Wands, 858 F.2d 731,736, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), as evidenced by the prior art teachings and Appellant's Specification. The amount of experimentation to practice the full scope of the claimed invention might have been extensive, but it would have been routine. The techniques necessary to do so were well known to those skilled in the art. Ex Parte Mar& Z. Kubin and Raymond G. Goodwin Appeal No. 2007-0819 (BPAI 2007)."

In this instance the state and knowledge of skill in the art, the relative skill in the art far exceeds any alleged unpredictability of the full scope of the claimed subject matter.

(A) Reply: It is acknowledged that, for US 09/667,859, Ex parte Kubin found that the genus of nucleic acid molecules "comprising a polynucleotide encoding a polypeptide at least 80% identical to amino acids 22-221 of SEQ ID NO: 2, wherein the polypeptide binds CD48" was enabled. It is acknowledged that said decision was based on the state of the art and the relative skill of those in the art.

However, the instant claims are not analogous to the claims of US 09/667,859 for the following reasons. First, the state of the art for detecting a polypeptide that binds CD48 was such that high through-put screening could have been used. In contrast, the instant specification fails to provide an assay for detecting a cysteine protease activity of the polypeptide of SEQ ID

NO: 2; no successful steps and reagents, including substrates of the polypeptide of SEQ ID NO: 2, are taught. Second, while the skill of the artisan in molecular biology is high, without guidance as to which residues of SEQ ID NO: 2 may, or may not be altered, and retain the desired activity, identifying active variants represents undue experimentation for reasons explained in the prior actions; see, especially the actions of February 3, 2009 (pg 9-10) and July 6, 2009 (pg 5-6).

Regarding the breath of the claims, the predictability of the art, the amount of direction/guidance, and working examples, the following comparisons are made. As explained in the action of 6, 2009 (pg 5-6), for the genera of polypeptides encompassed by 70% or 85% identity to SEQ ID NO: 2 herein, only 2.2×10^{-20}% and 3.7×10^{-13}%, respectively, would be active. In contrast, for the genera of polypeptides encompassed by 80% identity to amino acids 22-221 of SEQ ID NO: 2 in US 09/667,859, 6.1×10^{-6}% of the variants would be active. Techniques in the art such as high through-put mutagenesis and screening techniques would have allowed finding a few active mutants within several hundred thousand or up to about a million inactive mutants, as is the case for the genus of polypeptides encompassed by the claims of US 09/667,859. But finding a few mutants within several billion or more, as in the instant claims, would not be possible. As acknowledged by In re Kubin molecular biology is an unpredictable art (pg 14, parg 5). While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has not been provided in the instant specification. In addition, no examples, of any

variant having at least 80% identity to SEQ ID NO: 2 herein and having cysteine protease, are taught. Also, see below (B).

(B) Polynucleotides encoding a polypeptide with at least 70% or 85% homology to SEQ ID NO: 2 are enabled by the instant specification. Procedures and methods for identifying variant polynucleotides that retain the activity of the parental nucleotide are commonly practiced by a skilled artisan (i. e. advanced degree in biotechnology).

By using conventional tools, one of skill in the art can readily identify the region of the polynucleotide that encodes for the catalytic active site of SEQ ID NO: 2 and modify a parental nucleic acid without undue experimentation while retaining its catalytic activity characteristic of a cysteine protease. For example, Applicants have provided a GenBank protein domain analysis showing that the claimed polypeptide has an active site comprised of a histidine and cysteine diad which is characteristic of a cysteine protease (see, Office Action Response dated June 3, 2009, Exhibit A). Consequently, one having ordinary skill in the art would be able to practice Claims 1-4 and 17-21 without undue experimentation because they would be able to modify the claimed polynucleotides and polypeptides while maintaining the integrity (e.g., activity) of the cysteine protease domain.

(B) Reply: As explained above in (A), the instant specification fails to provide an assay for detecting a cysteine protease activity of the polypeptide of SEQ ID NO: 2; no successful steps and reagents, including substrates of the polypeptide of SEQ ID NO: 2, are taught.

It is acknowledged that Exhibit A shows that residues ~165-380 of SEQ ID NO: 2 has structural homology to the peptidase C1A super-family. However, said structural homology is

not to a protein demonstrated to have a well-established utility as a cysteine protease but to a database based on structural homology among protease. As stated by Rawlings et al, 2010, MEROPS is a collection of protease clans and families, which were constructed based on homology to a single well-characterized protease example to which other proteins are compared (pg D227, parg 2). Thus, each clan/family is a collection of sequences having some structural similarity, the vast majority of which have no well-established activity. No assertion is made by MEROPS that one can conclude the function of a protein based on homology to a clan or family (Examiner's emphasis)."

It is well known in the art that development of protein databases that annotate the "function" of a protein based solely on homology has led to an iterative "transitive identification catastrophe", wherein protein "A" has the specific function, but serial homology analysis does not provide confidence that protein "Z" in the series has the same function (Barker et al, 2001). As explained above, the authors of MEROPS assert only that their analysis of known sequences is a means to divide proteins into structurally similar categories; no assertion of functional relationships has been made. The skilled artisan would not conclude based solely on homology to such a database that, more likely than not, a new protein has the annotated activity.

For these reasons and those explained in the prior action, rejection of Claims 1-4 and 17-21 under 35 U.S.C. 112, first paragraph/enablement, is maintained.

Written Description

Rejection of Claims 1-4 and 17-21 under 35 U.S.C. 112, first paragraph/written description, for the reasons explained in the prior action, is maintained.

In support of their request that said rejection be withdrawn, Applicants provide the following arguments. The feature of having a cysteine protease active site correlates the structure of the claimed polypeptides with their function as a cysteine protease. Notably, the claimed sequences are drawn to polynucleotides encoding a polypeptide with cysteine protease activity. As such, the potential genus is not as large as asserted by the Examiner.

This argument is not found to be persuasive because the specification fails to teach that the polynucleotide of SEQ ID NO: 1, or any variant thereof, encodes a protein having the recited activity. The specification also fails to teach the active site of the protein of SEQ ID NO: 2. The skilled artisan would not recognize that Applicants were in possession of the genus of all proteins having at least 70% or 80% identity with SEQ ID NO: 2 and having cysteine protease activity.

For these reasons and those explained in the prior action, rejection of Claims 1-4 and 17-21 under 35 U.S.C. 112, first paragraph/written description, is maintained.

Allowable Subject Matter

No claims are allowable.

Applicant's amendment necessitated any new grounds of rejection presented in this Office action. Any new references were cited solely to support rejection(s) based on amendment or rebut Applicants' arguments. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Regarding filing an Appeal, Applicants are referred to the Official Gazette Notice published July 12, 2005 describing the Pre-Appeal Brief Review Program.

Final Comments

To insure that each document is properly filed in the electronic file wrapper, it is requested that each of amendments to the specification, amendments to the claims, Applicants' remarks, requests for extension of time, and any other distinct papers be submitted on separate pages. It is also requested that the serial number of the application and date of amendment be referenced on every page of the response.

It is also requested that Applicants identify support, within the original application, for any amendments to the claims and specification.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 571-272-0943. The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published application may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on the access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/SHERIDAN SWOPE/
Primary Examiner, Art Unit 1652